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83-790688/42 B04 D16 J04 K08 INSP 12.03.82
INST PASTEUR (CNRS) *FR 2523-311-A
12.03.82-FR-004247 (16.09.83) G01n 33/66 C07g 07/00
B(4-B2C, 4-[illegible], 4-B4A, 4-B4C, 4-B4D, 4-B4F, 5-A4, 11-C7A, 11-C7B, 12-K4) D(5-A1, 5-H) J(4-B1) 001

Aq.- soluble albumin-ligand coupling product - for use in immunoassays

C83-102376 Issued in Week 8343.
Full Patentees: Inst. Pasteur; Cent. Nat. Rech. Scientifique.

(A) an albumin/specific ligand coupling prod. which is soluble in aq. media is new.

(B) Immunoassay of a biological substance (I) comprises (a) immobilising a substance (II) having binding affinity for (I), (b) incubating with a medium contg. (I), (c) washing the resulting reaction mixt. and incubating with an albumin/specific ligand coupling prod. in soln. in an aq. medium, where the ligand is capable of reacting specifically with (I) or (II), (d) washing the resulting reaction mixt. and incubating with a labelled anti-albumin antibody, and (e) detecting the label.

(C) An immunoassay test kit comprises an albumin/specific ligand coupling prod., a labelled anti-albumin antibody and reagents for detecting the label.

ADVANTAGES

Coupling with albumin increases sensitivity, esp. in the case of enzyme immunoassays for antigens, haptens or antibodies.

DETAILS

The specific ligand may be an antigen, hapten, antibody, hormone, hormone receptor, enzyme inhibitor or lectin. It may be coupled with human or animal albumin (esp. BSA) using glutaraldehyde or by 2-stage benzoquinone activation and coupling.

The label may be an enzyme, a radioactive material, a fluorochrome, a particulate material or erythrocytes.

EXAMPLE

A BSA/anti-IgE reagent was prepd. by isolating sheep anti-rabbit Ig antibodies by affinity chromatography, dialysing the antibodies and BSA against phosphate buffer (0.1 M, pH 6.8) at 4°C overnight, and mixing 3 mg of the dialysed antibody with 6 mg of the dialysed BSA in 0.1M phosphate buffer. The mixt. (1 ml) was treated with 0.2 ml of 1% aq. glutaraldehyde and incubated at room temp. for 3 hr.

The prod. was used in a sandwich-type enzyme immunoassay for human IgE.(18pp367EDDwgNo0/0).

FR2523311-A

83-795400/43 B07 P34 HEYM/ 01.03.82
HEYMAN A M *AU 8311-382-A
18.05.82-US-379480 (+US-353432) (08.09.83) A61m-29
B(11-C4B) 002

Urological instrument esp. retentive balloon catheter - inserted by sliding over filiform

C83-102379 A urological instrument (esp. a catheter) is inserted into the bladder by first advancing a filiform through the urethra, the filiform having smoothly contoured leading end with a lateral opening. Urine flows through this opening and into the filiform to indicate when the leading end of the filiform has entered the bladder.

The urological instrument has an internal dia. greater than the external dia. of the filiform to permit the instrument to be slid along the filiform. The instrument may have an inflatable balloon collar which retains the instrument in the bladder; the filiform can then be withdrawn.

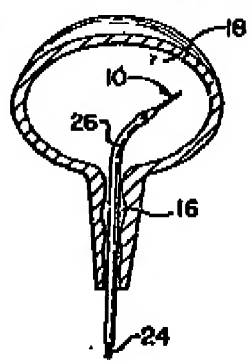
ADVANTAGE

The correct positioning of the filiform is indicated by the drainage of urine.

EMBODIMENT

Bladder (18) has the drainage catheter (26) in position. Pref. the leading section of the filiform (10) is curved as shown.

The filiform may be inserted while a stylet wire extends axially within the filiform to stiffen it. Similarly, a stylet tube (24) is placed inside the drainage catheter while it is being slid along the pre-positioned filiform.(25pp295GHDwgNo5/6)



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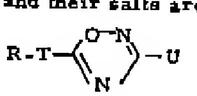
83-795403/43 B03 (B02) SUMO 03.03.82
SUMITOMO CHEMICAL KK *AU 8311-483-A
03.03.82-JP-034168 (08.09.83) A61k-31/41 C07d-271/06 C07d-413/04 C07d-417/10 C07d-471/04 C07d-491/05
B(6-H, 7-E4, 12-D1, 12-D7, 12-D8) 003

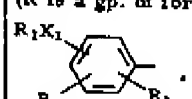
5-Aralkyl-1,2,4-oxadiazole derivs. - are antiinflammatories, analgesics and antipyretics

C83-102382 5-Aralkyl-1,2,4-oxadiazole derivs. of the formula (I) and their salts are new



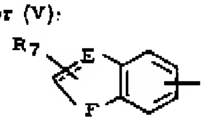
(I)

(R is a gp. of formula (II), (III), (IV) or (V):

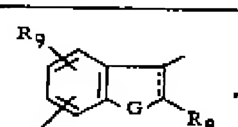


(II)

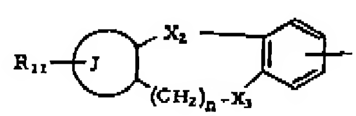
(III)



(IV)



(V)



(VI)

R_1 is alkyl, alkenyl, cycloalkyl, cycloalkenyl, opt. substd. phenyl or heterocyclyl;
R_2 and R_3 are each H, halo, amino, OH, alkoxy or alkyl;
X_1 is $-CH_2-$, $-CH_2O-$, -CO-, -O-, -S-, -NH or a single bond;
R_4 and R_5 are H alkyl or opt. substd. phenyl;
R_6 is opt. substd. phenyl or opt. substd. benzoyl;
A is N, O or S;
B and D are each C or N;
R_7 is alkyl, lower alkoxy or opt. substd. phenyl;
E is N or C;
F is O, S or C or C=C or C=N,
broken lines indicate opt. bonds;
R_8 is H or lower alkyl;

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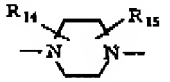
R_9 is H, halo or alkoxy;
R_{10} is H, cyclohexyl or substd. benzoyl;
G is methylene, substd. benzoylimino, cinnamoylimino or substd. styrylidene, provided that G is $-CH_2-$ when R_{10} is cyclohexyl or substd. benzoyl;
R_{11} is H, halogen, alkyl or alkoxy;
X_2 and X_3 are different and are $-CH_2-$, -CO-, -O-, -S-, -NH- $-N(CH_3)-$ or single bond;
J is a benzene, pyridine, thiophene, furan or pyrrole ring;
n is 0 or 1;
T is alkylene or alkenylene each opt. carrying an oxo, OH or lower alkoxy substit., or T is a single bond;
U is H, alkyl, alkenyl, polyhaloalkyl, cycloalkyl, cycloalkenyl, opt. substd. phenyl, pyridyl, $-T_1-R_{12}$ or $R_{13}-X_4-T_2-$;
R_{12} is halogen, OH, SH, alkylsulphinyl, dialkoxymethyl, alkoxycarbonyl, COOH, sulpho, CN, NR'R" or $-\overset{\oplus}{S}R_1'R_1''.X^{\ominus}$;
R' and R" are H, alkyl or hydroxyalkyl;
or NR'R" forms a 5 or 6 membered opt. unsatd. heterocyclic ring, which may contain an O or another N atom, or forms a quaternary ammonium salt or N-oxide;
R_1' or R_1'' are alkyl or alkenyl;
X is negative monovalent ion;
T_1 is alkylene or alkenylene, opt. bearing an OXO or OH substit.;
R_{13} is alkyl, alkenyl, hydroxyalkyl, acyloxyalkyl, amino alkyl, acylaminoalkyl, cycloalkyl, cycloalkenyl, opt. substd. phenyl, phenyl-alkyl, heterocyclyl, heterocyclyl-alkyl, acyl, acylthioalkanoyl, mercaptoalkanoyl, alkoxycarbonyl, alkylsulphonyl, $-CONR_2'R_2''$ or $SO_2NR_2'R_2''$;
R_2' and R_2'' are each H, alkyl or hydroxyalkyl;
X_4 is -O-, -S-, -NH-, a single bond or a gp. of formula (VIII)



(VIII)

R_{14} and R_{15} are each H or alkyl.
All alkyl, alkenyl, alkylene, alkenylene, cycloalkyl and cycloalkenyl gps. are 'lower' i.e. ≤ 6C; and cycloalkyl gps. may be oxo- or hydroxy-substd.).

USE

(I) are antiinflammatories, analgesics and antipyretics without ulcerogenic side effects.

PREPARATION

By several methods including:-

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1) R-T-COOH (or reactive ester) (II) + HON=C(-U)-NH_2 (III) → R-T-C(=O)-O-N=C(-U)-NH_2 (IV) → (I)

2) R-T-CN (V) + O←N≡C-U_1 → (I; U = U_1)

(U_1 is alkyl, alkenyl, polyhaloalkyl, cycloalkyl, cycloalkenyl, phenyl, substd. phenyl, pyridyl or $R_{16}-T_2-$;
T_2 is alkylene or alkenylene;
R_{16} is halogen, alkoxy, alkenyloxy, dialkoxy) methyl carboxy, cycloalkyl, phenyl, substd. phenyl, pyridyl, NR'R", $CONR_2'R_2''$ or $-SO_2NR_2'R_2''$).

3) R-T-CONHCSU_1 $\xrightarrow{H_2NOH}$ (I; U = U_1)

4) RO-T_1-CHO + HON=C(-U_1)-NH_2 → RO-T_1-(oxadiazole)-U_1 (Ib)

oxidn. → RO-T_1-(oxadiazole)-U_1

(Ro is same as R provided X_1, X_2 and X_3 are not -S-)

EXAMPLE

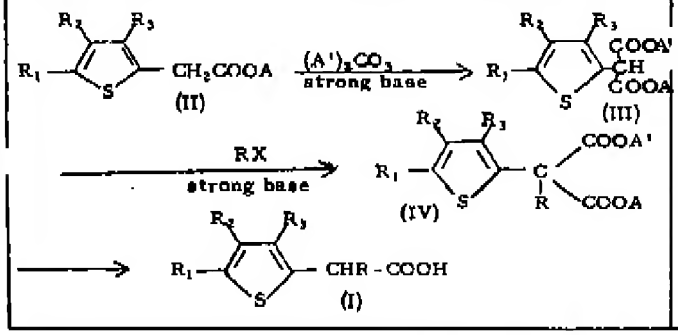
A mixt. of 2-(2-fluoro-4-biphenylyl)propionic acid (2.44 g), dry benzene (50 ml) and thionyl chloride (2.38 g) was refluxed for 2 hr., concd. under reduced pressure and residue dissolved in dry benzene (5 ml). The soln. was added dropwise with cooling to a soln. of acetamidoxime (0.815 g) in dry pyridine and stirred at room temp. and refluxed for 5 hr. The solvent was evapd. under reduced pressure and the residue partitioned between benzene (100 ml) and 10% Na_2CO_3 soln. (20 ml). The organic phase was washed, dried and evapd. and the residue chromatographed on silica gel and eluted with benzene to give 5-(3-fluoro-4-phenyl-α-methylbenzyl)-3-methyl-1,2,4-oxadiazole which was recrystallised from n-hexane to give product (m.p. 55-56°C). (99pp916EDDwgNo0/0).

83-795403/43(3) AU8311483-A

83-795432/43 B03 ROUS 03.12.82
ROUSSEL UCLAF *BE -896-439-A
03.12.82-FR-020271 (12.10.83) C07d

Alpha-alkyl 2-thienyl acetic acid derivs. prodn. - by reacting 2-thienyl acetic acid with alkyl carbonate alkylating agent, then decarboxylation

C83-102391 (I) Prodn. of α-alkyl- 2-thienylacetic acid derivs. of formula (I) by the following process is new:



(II) → (III) → (IV) → (I)

B(7-81) 004

(R is 1-4C alkyl;
R_1, R_2 and R_3 are each H, 1-4C alkyl or halo;
A and A' are 1-4C alkyl; and
X is a functional gp).
(2) The 2-(1,1-di(alkoxycarbonyl)-alkyl)-thiophene intermediates of formula (IV) are new cpds.

USE

(I) are intermediates for pharmaceuticals, esp. antiinflammatories.

ADVANTAGES

The process uses fewer stages than known methods.

DETAILS

The first stage is pref. in presence of Na ethoxide (esp. 1-1.5 equiv. per mole (II)) at 90-135°C. Reaction of (IV is esp. also in presence of Na ethoxide, at 50-80°C.

The final stage is by hydrolysis with base, esp. at 50°C to reflux, then acidification with HCl.

The method is esp. used to make (I) where R_1 = R_2 = R_3 = H and R = methyl, cpd. (Ia).

EXAMPLE

BE 896439 -A+